Chapter 14

Anesthesia for Myocardial Revascularization

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Key Points

1. Guideline updates emphasize the efficacy of surgical approaches to myocardial revascularization in patients with multivessel coronary artery disease.
2. Perioperative risk reduction includes careful consideration of all of the patient's relevant antihypertensive, antiplatelet, and antianginal medications.
3. Significant valvular abnormalities in patients scheduled for coronary revascularization should be evaluated and considered in surgical planning.
4. Off-pump coronary artery bypass surgery is an established alternative to on-pump myocardial revascularization (ie, coronary artery bypass grafting [CABG]). The choice and outcomes of either approach are highly surgeon dependent. Despite apparent advantages of avoiding cardiopulmonary bypass (CPB), evidence from large prospective trials enrolling mostly low-risk patients has not shown clear reductions in mortality with an off-pump approach.
5. Possible indications for pulmonary artery catheter use in CABG surgery include patients with pulmonary hypertension, right-sided heart failure, or severely impaired ventricular function, particularly those who require postoperative cardiac output monitoring.
6. Fast-tracking, including early extubation and mobilization, has been almost universally adopted for patients undergoing myocardial revascularization.
7. Anesthetic drugs, especially inhaled anesthetic agents, may help to ameliorate myocardial injury associated with CPB and aortic cross-clamping by their preconditioning and postconditioning effects. However, the magnitude of these effects on outcome remains controversial.

The role of the cardiac anesthesiologist in the perioperative care of patients undergoing myocardial revascularization continues to evolve. Achievements of the past two decades include providing safe anesthesia that allows rapid recovery and optimizing monitoring that includes the establishment of transesophageal echocardiography (TEE) as a standard of care in the cardiac operating room. More recent developments in patient care include the introduction of a perioperative surgical home, which affects the management of patients undergoing myocardial revascularization. The anesthesiologist is vitally important in the multidisciplinary approach to patient care. Optimal perioperative care requires close collaboration and coordination between the various specialties involved on the heart team. The process begins with the decision to proceed to surgery and continues with preoperative optimization, state-of-the-art perioperative and postoperative care, and rehabilitation after hospital discharge. Beyond safe anesthesia technique, the anesthesiologist must be well versed in all areas of perioperative management for patients with coronary artery disease (CAD). This includes advances in pharmacologic risk reduction, new surgical techniques, and anesthetic management and monitoring techniques to improve patient outcomes.

EPIDEMIOLOGY

According to the American Heart Association Heart Disease and Stroke Statistics, most recently updated in 2014, epidemiologic data relevant to cardiovascular disease can be summarized as follows. Overall rates of death attributable to cardiovascular disease have declined 31%; for CAD, there was a 39.2% decrease from 2000 to 2010. This was partially attributed to improvements in acute treatment of patients with acute coronary syndromes (ACSs), secondary preventive therapies after myocardial infarction (MI), treatment of acute heart failure (HF), revascularization of chronic CAD, and other preventive therapies. However, the prevalence remains high, with cardiovascular disease accounting for 31.9% of all deaths in the United States. Based on current estimates, by 2030 43.9% of the US population will have some form of cardiovascular disease. Similarly, 15.4 million individuals had CAD in 2010; and ischemic heart disease causes approximately one of every six deaths in the United States. In 2010, 379,559 Americans died of CAD, and statistically, every 34 seconds one person in the United States has a coronary event.

Between 2000 and 2010 the total number of inpatient cardiovascular procedures in the United States increased by 28%, with a total of 7,588,000 cardiovascular procedures performed in 2010. In 2010 an estimated 219,000 patients underwent 397,000 coronary artery bypass graft (CABG) procedures (Fig. 14.1). The in-hospital mortality rate for CABG declined by 50% despite an increase in the comorbidity index. CAD alone resulted in more than $44 billion in expenses, making it the most expensive condition treated. The total direct and indirect cost of cardiovascular disease and stroke was estimated to be $315.4 billion in 2010, more than for any other diagnostic group.

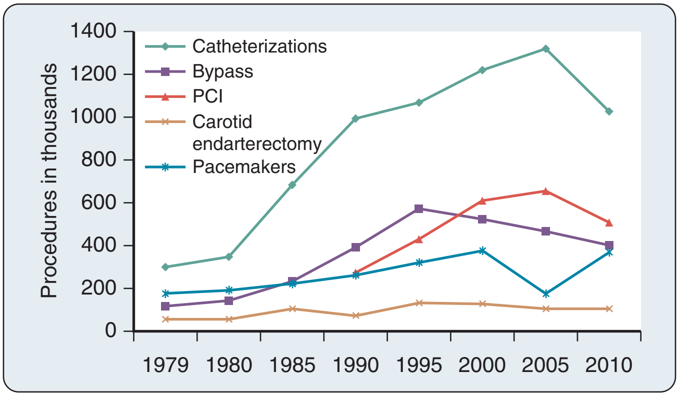


Fig. 14.1 Trends in cardiovascular operations and procedures from 1979 to 2010 for inpatient procedures only. *PCI*, Percutaneous coronary intervention. (From Mozaffarian D, Benjamin EJ, Go AS, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics: 2015 update. A report from the American Heart Association. *Circulation.* 2015;131:e29.)

PATHOPHYSIOLOGY OF CORONARY ARTERY DISEASE

Anatomy

The anesthesiologist should be familiar with coronary anatomy if only to interpret the significance of angiographic findings. The coronary circulation and common sites for placement of distal anastomoses during CABG are shown in Figs. 14.2 through 14.4.

The right coronary artery (RCA) arises from the right sinus of Valsalva and is best seen in the left anterior oblique view on coronary cine angiography. It passes anteriorly for the first few millimeters and then follows the right atrioventricular (AV) groove and curves posteriorly within the groove to reach the crux of the heart, the area where the interventricular septum (IVS) meets the AV groove. In 84% of cases, it terminates as the posterior descending artery (PDA), which is its most important branch because it is the sole supply to the posterosuperior IVS. Other important branches are those to the sinus node in 60% of patients and the AV node in approximately 85% of patients. Anatomists consider the RCA to be dominant when it crosses the crux of the heart and continues in the AV groove regardless of the origin of the PDA. Angiographers, however, ascribe dominance to the artery—right coronary or left coronary (ie, circumflex)—that gives rise to the PDA.

The vertical and superior orientation of the RCA ostium allows easy passage of air bubbles during aortic cannulation, cardiopulmonary bypass (CPB), or open valve surgery. In sufficient volume, myocardial ischemia involving the inferior left ventricular (LV) wall segments and the right ventricle may occur (Fig. 14.5). In contrast, the

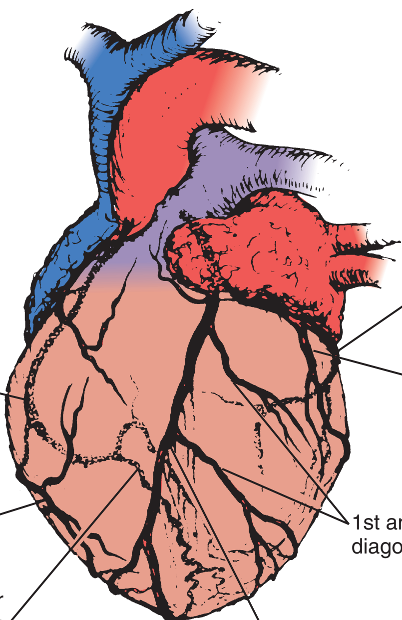


Fig. 14.2 Thirty-degree left anterior oblique angiographic view of the heart, which best shows the right coronary artery. *Lines* indicate common sites of distal vein graft anastomoses. (From Stiles QR, Tucker BL, Lindesmith GG, et al. *Myocardial Revascularization: A Surgical Atlas.* Boston, Little, Brown; 1976.)

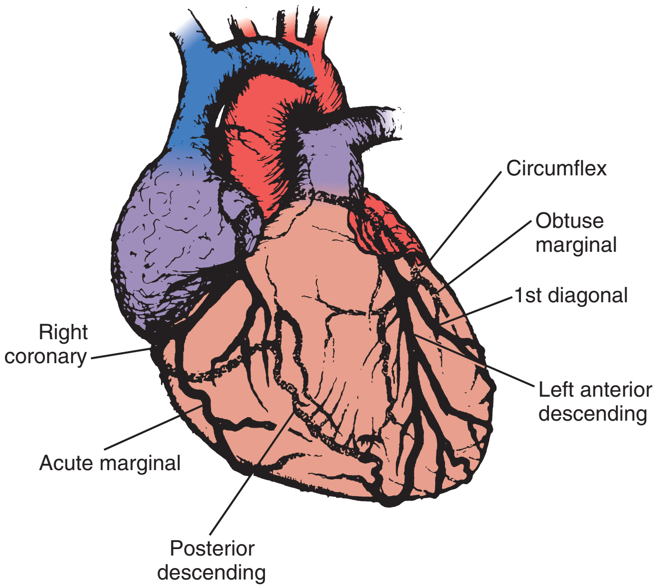


Fig. 14.3 Ten-degree right anterior oblique angiographic view of the heart, which best shows the left main coronary artery dividing into the circumflex and left anterior descending arteries. *Lines* indicate common sites of distal vein graft anastomoses. (Modified from Stiles QR, Tucker BL, Lindesmith GG, et al. *Myocardial Revascularization: A Surgical Atlas*. Boston: Little, Brown; 1976.)

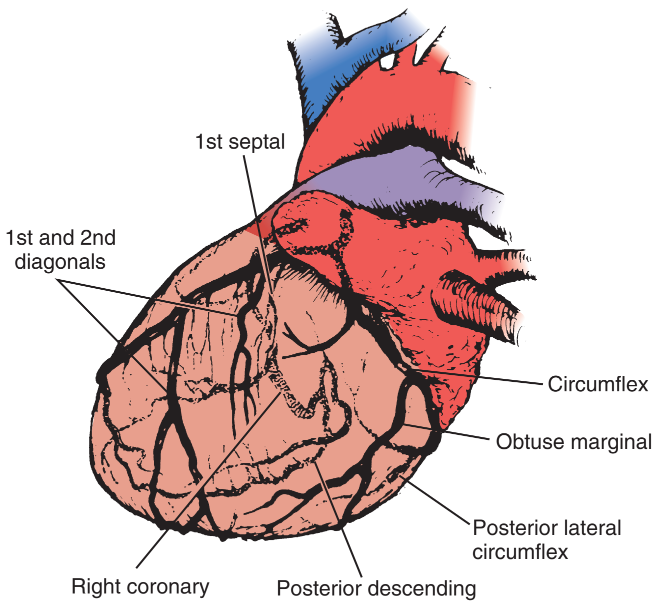


Fig. 14.4 Seventy-five–degree left anterior oblique angiographic view of the heart, which best shows branches of the left anterior descending and circumflex coronary arteries. *Lines* indicate common sites of distal vein graft anastomoses. (Modified from Stiles QR, Tucker BL, Lindesmith GG, et al. *Myocardial Revascularization: A Surgical Atlas.* Boston: Little, Brown; 1976.)

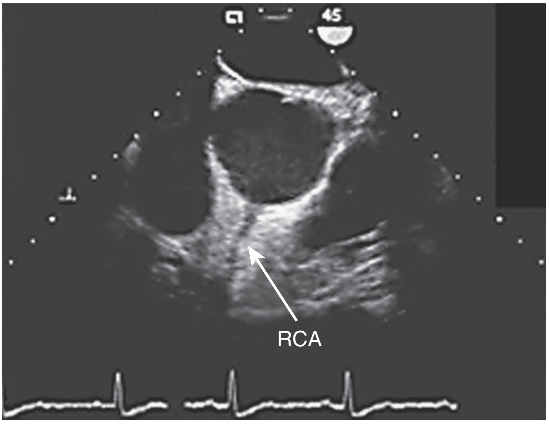


Fig. 14.5 The vertical and superior orientation of the right coronary artery *(RCA)* arising from the aortic root is identified by transesophageal echocardiography (TEE). The TEE transducer in the esophagus is at the top of the screen, and the patient's chest wall is at the bottom. Retained air preferentially enters the RCA, which may cause inferior ischemia, depending on the amount of air and the coronary perfusion pressure. Elevation of perfusion pressure using phenylephrine is often used to treat coronary air embolus. The left main coronary artery (not visible) arises at approximately 3 o'clock on this image. (Courtesy Martin J. London, MD, University of California, San Francisco, CA *[www.ucsf.edu/teeecho].)*

near-perpendicular orientation of the left main coronary ostium makes air embolization much less common.

The left coronary artery arises from the left sinus of Valsalva as the left main coronary artery. It is best seen in a shallow right anterior oblique projection (see Fig. 14.3). The left main coronary artery courses anteriorly and to the left, where it divides in a space between the aorta and pulmonary artery. Its branches are the left anterior descending (LAD) artery and circumflex artery. The LAD passes along the anterior interventricular groove. It may reach only two-thirds of the distance to the apex or extend around the apex to the diaphragmatic portion of the left ventricle. Major branches of the LAD are the diagonal branches, which supply the free wall of the left ventricle; and septal branches, which course posteriorly to supply the major portion of the IVS. Although there may be many diagonal and septal branches, the first diagonal and first septal branches serve as important landmarks in the descriptions of lesions of the LAD.

The circumflex artery arises at a sharp angle from the left main coronary artery and courses toward the crux of the heart in the AV groove. When the circumflex artery gives rise to the PDA, the circulation is left dominant, and the left coronary circulation supplies the entire IVS and the AV node. In approximately 40% of patients, the circumflex artery supplies the branch to the sinoatrial node. Up to four obtuse marginal (OM) arteries arise from the circumflex artery and supply the lateral wall of the left ventricle.

All of the previously described epicardial branches give rise to small vessels that supply the outer third of the myocardium and penetrating vessels that anastomose with the subendocardial plexus. The capillary plexus is unique in that it functions as an end-arterial system. Each epicardial arteriole supplies a capillary plexus that forms an end loop rather than anastomosing with an adjacent capillary from another epicardial artery. Significant collateral circulation does not exist at the microcirculatory level. The capillary anatomy explains the distinct areas of myocardial ischemia or infarction that can be related to disease in a discrete epicardial artery. CAD most commonly

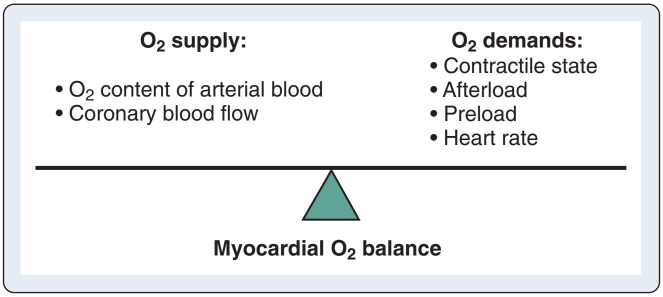


Fig. 14.6 Factors determining myocardial oxygen supply and demand.

affects the epicardial muscular arteries with rare intramyocardial lesions (with the exception of the transplanted heart). However, severe disorders of the microcirculation and primary impairment of coronary vascular reserve in normal coronary arteries have been described, especially in patients with diabetes, females, and those with variant angina. Epicardial lesions can be single but are more often multiple. A combined lesion of the RCA and both branches of the left coronary artery is referred to as *triple-vessel disease*. Venous drainage of the myocardium primarily occurs through the coronary sinus, which enters the right atrium between the inferior vena cava and the tricuspid valve. A small fraction enters the cardiac chambers directly through the Thebesian veins.

Myocardial Ischemia and Infarction

In patients with CAD, myocardial ischemia usually results from increases in myocardial oxygen demand exceeding the capacity of the stenosed coronary arteries to increase oxygen supply (Fig. 14.6). In atherosclerotic heart disease, the fundamental lesion is an intimal lipid plaque in the epicardial portion of a coronary artery that causes chronic stenosis and episodic thrombosis and sudden plaque rupture that results in almost complete occlusion. Characteristics of the vulnerable plaque include a high lipid content, a thin fibrous cap, a reduced number of smooth muscle cells, and increased macrophage activity. Chronic inflammation and acute processes such as a plaque rupture result in the release of vasoactive substances from platelets and leukocytes producing endothelial dysfunction and vasoconstriction and further reducing coronary blood flow (CBF). A larger plaque disruption and prolonged thrombosis produce a Q-wave infarction with transmural myocardial necrosis.

Collateral vessels exist in normal hearts, but in the setting of CAD, they are increased in size and number. Collaterals may develop between the ischemic zone and an adjacent nonischemic area supplied by a different vessel. Although beneficial at rest, during exercise or periods of increased oxygen demand, CBF may be shunted away from the ischemic myocardium to areas with intact autoregulation able to vasodilate; this is referred to as a *coronary steal*.

ANESTHESIA FOR CORONARY ARTERY BYPASS GRAFTING

The practitioner providing anesthesia care for patients undergoing coronary revascularization has to implement an anesthetic plan that takes patient- and surgery-specific factors into consideration, but it should also include the most recent recommendations and guidelines regarding the perioperative care of patients with CAD.

In the earlier days of cardiac surgery, the focus on anesthesia management for patients undergoing CABG was mainly on maintaining hemodynamic stability and preventing ischemia. This reflected the lack of anesthetic agents with minimal hemodynamic effects. Later reports supported a lack of effect of the technique, suggesting that hemodynamic control was more important (ie, it is not what you use, but how you use it). With the introduction of modern anesthetic agents, the focus shifted to investigating how the various regimens and techniques could help to improve outcomes of patients undergoing myocardial revascularization. For example, considerable data demonstrate the beneficial effects of using potent inhalation agents or sympathetic blockade on markers of myocardial ischemia and postoperative MI, such as improved recovery and shorter length of stay (LOS).

Premedication

The concept of premedication has been evolving beyond the traditional ordering of sedative-hypnotics or related agents to reduce patient anxiety and promote amnesia. The cardiac anesthesiologist must be familiar with the potential benefits of administering or hazards of not administering a variety of medications, including antianginal, β-blocker, and antiplatelet drugs.

Anxiolysis, Amnesia, and Analgesia

The purposes of premedication are to pharmacologically reduce apprehension and fear, to provide analgesia for potentially painful events before induction (eg, vascular cannulation), and to produce some degree of amnesia. In patients with CAD, premedication may help prevent preoperative anginal episodes that are relatively commonly observed and may be elicited by tachycardia due to anxiety or painful stimuli. Short-acting benzodiazepines are the mainstay of drugs administered for this purpose. When given intravenously in the preoperative holding area to patients with CAD, supplemental oxygen should be administered and the patients monitored by pulse oximetry, an electrocardiogram (ECG), and noninvasive blood pressure (BP) methods.

Management of Preoperative Medications

Patients undergoing myocardial revascularization routinely take medications aiming to prevent acute coronary events, worsening of ischemia, or HF symptoms. Many of these drugs have implications for anesthesia management, and the anesthesiologist should be familiar with the current guidelines and recommendations outlining their use in the perioperative setting (Box 14.1).

β-BLOCKING AGENTS

β-Blocking agents are routinely administered to many patients with CAD. As early as the mid-1970s, Kaplan suggested that it was safe to continue β-blockade in patients with ischemic heart disease undergoing cardiac or noncardiac surgery, even those with poor ventricular function. This was confirmed in many prospective, randomized trials that established the safety of continuing β-blockade in the perioperative period.

In a metaanalysis, Wiesbauer et al. found that perioperative β-blockers reduced perioperative arrhythmias after cardiac surgery, but they were unable to show an effect on MI or mortality. Based on the existing evidence from a few randomized, controlled trials, retrospective studies, and metaanalyses, β-blocker use was recommended by many specialty societies for patients undergoing CABG.

The 2011 American College of Cardiology Foundation and American Heart Association (ACCF/AHA) guideline for CABG surgery recommended that β-blockers should be administered for at least 24 hours before CABG to all patients without

BOX 14.1 ***Preoperative Medication Management***

1. β-Adrenergic blockers
   - Should be administered for at least 24 hours before coronary artery bypass grafting (CABG) to all patients without contraindications (eg, hypotension, third-degree heart block, bronchospasm).
   - After CABG surgery, should be reinstituted as soon as possible in all patients without contraindications.
2. Statins: All patients undergoing CABG should receive them unless contraindications apply.
3. Calcium channel blockers: Patients already on calcium channel blockers should continue them perioperatively.
4. Angiotensin-converting enzyme inhibitor:
   - Preoperative discontinuation is controversial (ie, increased risk of hypotension and vasoplegic syndrome).
   - Postoperatively, should be initiated and continued indefinitely in CABG patients who are stable unless contraindications apply.
5. Diuretics: No firm recommendations, but ensure adequate serum potassium levels.
6. Aspirin: Should be administered preoperatively. The decision about whether and when to discontinue aspirin before surgery depends on patient-specific factors such as individual risk for bleeding and presence of an acute coronary syndrome. Postoperatively, aspirin should be started as early as possible (ie, within 6 to 24 hours after surgery).
7. Antiplatelet agents such as oral inhibitors of purinergic receptor P2Y12: Because they are associated with an increased risk of bleeding, recommendations call for withholding for a few days before surgery. However, in high-risk patients and/or after placement of drug-eluting stents, recommendations may change, and intravenous glycoprotein IIb/IIIa inhibitors or cangrelor may be continued perioperatively despite increased risk of bleeding.
8. Heparin: Regimen often depends on the surgeon. Usually discontinued 4 hours preoperatively for stable patients, continued up to and through pre–cardiopulmonary bypass period for critical left main disease or acutely unstable angina patients.
9. Oral hypoglycemic agents: No firm recommendations; consider withholding administration. However, glucose control must be ensured.
10. Antibiotic prophylaxis: Optimal timing and weight adjustment (especially important with antibiotics that have slow tissue penetration such as vancomycin). Typically, a second-generation cephalosporin such as cephazolin (2 g IV) or cefuroxime (1.5 g IV) administered 20 to 60 minutes before incision; vancomycin (15 mg/kg) administered as a slow infusion to avoid hypotension and flushing (owing to slow tissue penetration, infusion should be completed 20 to 30 minutes before skin incision).

contraindications to reduce the incidence or clinical sequelae of postoperative atrial fibrillation (AF). The guidelines state that β-blockers in patients with CABG with an ejection fraction (EF) greater than 30% can be effective in reducing the risk of in-hospital mortality and the incidence of perioperative myocardial ischemia. In patients with severely depressed LV function (EF <30%), the effectiveness of preoperative β-blockers in reducing the in-hospital mortality rate is uncertain. After CABG, β-blockers should be reinstituted as soon as possible for all patients without contraindications.

In 2015, the AHA published a scientific statement complementing the existing guidelines that focused on secondary prevention measures after CABG. The expert statement supports the recommendation to give β-blockers starting before surgery, including administering them to patients with prior MI unless contraindicated (eg, bradycardia, severe reactive airway disease). In patients with previous MI, β-blockers are specifically recommended for patients with HF symptoms and an EF below 40%.

ANTIPLATELET DRUGS

In accordance with current guidelines, most patients undergoing CABG are treated with platelet inhibitors. Aspirin is a well-recognized component of primary and secondary prevention strategies for all patients with ischemic heart disease. Clopidogrel administration is established practice after coronary artery stent placement, and it is recommended in combination with aspirin for patients with ACS.

Guidelines summarizing the current evidence regarding antiplatelet drugs in patients undergoing surgery have been published by various specialty societies and are updated regularly. The most recent update of The Society of Thoracic Surgeons guidelines on the use of antiplatelet drugs in patients undergoing CABG was published in 2012. The highest level of evidence (class I recommendation, level A evidence) was found for aspirin administration within 6 to 24 hours after surgery in nonbleeding patients to optimize vein graft patency, and for dual antiplatelet therapy for patients undergoing CABG after ACS as soon as the bleeding risk is diminished to decrease adverse cardiovascular outcomes. The class I recommendation with level B evidence advised discontinuing inhibitors of the receptor P2Y12 for a few days before surgery to reduce the risk of bleeding and need for blood transfusion.

The 2011 ACCF/AHA guideline for CABG surgery recommended that aspirin should be administered to CABG patients preoperatively. For elective CABG, clopidogrel and ticagrelor should be discontinued for at least 5 days before surgery and prasugrel for at least 7 days to limit the need for blood transfusions. For urgent surgery, clopidogrel and ticagrelor should be discontinued for at least 24 hours to reduce major bleeding complications. Postoperatively, aspirin should be started within 6 hours after surgery. For those allergic to aspirin, clopidogrel should be used instead. Low-dose aspirin should be continued indefinitely. The 2015 AHA scientific statement on secondary prevention measures after CABG confirmed these recommendations and recommended dual antiplatelet therapy with aspirin and clopidogrel for 1 year.

HMG COA REDUCTASE INHIBITORS

Potent antiinflammatory and antithrombotic effects and beneficial effects on endothelial function and angiogenesis have been reported for 3-hydroxy-3-methyl-glutaryl–coenzyme A (HMG CoA) reductase inhibitors (ie, statins). Improved outcomes also have been described for patients undergoing CABG. This includes attenuation of myocardial reperfusion injury after CPB, reducing short- and long-term mortality rates, and decreasing early graft occlusion in patients with CABG.

Based on the accumulating evidence for the beneficial effects of statin therapy in patients undergoing myocardial revascularization, guidelines have been adjusted. The 2011 ACCF/AHA guideline for CABG surgery recommended that, unless contraindications apply, all patients undergoing CABG should receive statin therapy with the goal of lowering low-density lipoprotein (LDL) cholesterol by at least 30% or to less than 100 mg/dL. Even lower targets may be advisable (<70 mg/dL) for very high-risk patients. The most recent AHA scientific statement on secondary prevention measures after CABG confirmed these recommendations, and recommended statin therapy starting preoperatively and continued after surgery.

ANGIOTENSIN-CONVERTING ENZYME INHIBITORS

Angiotensin-converting enzyme (ACE) inhibitors are widely considered to be vasculoprotective, particularly with regard to ventricular remodeling after acute MI, and they appear to reduce damage after ischemic reperfusion. The role of ACE inhibitors in improving major outcomes for patients with ischemic heart disease and those undergoing myocardial revascularization has been investigated.

The 2011 ACCF/AHA guideline for CABG surgery recommended that preoperative use of ACE inhibitors and angiotension II receptor blockers (ARBs) should prompt reinstitution postoperatively after the patient is stable unless contraindicated. Independent of preoperative use, ACE inhibitors and ARBs should be initiated postoperatively and continued indefinitely in patients with CABG who are stable unless contraindications apply. The task force also acknowledges that the safety of the preoperative ACE inhibitors or ARBs in patients on chronic therapy is uncertain. The most recent AHA scientific statement on secondary prevention measures after CABG confirmed these recommendations and recommended administering ACE inhibitors or ARB therapy after CABG to all patients with LV dysfunction.

Monitoring

Electrocardiogram

On arrival in the operating room, the patient undergoing CABG should have routine monitors placed, including pulse oximetry, noninvasive BP, and the ECG. A five-lead system is standard for patients undergoing cardiac surgery. Monitoring leads V_5 and II allows detection of 90% of ischemic episodes and assessment of the rhythm to diagnose various atrial and ventricular arrhythmias (Box 14.2).

BOX 14.2 ***Intraoperative Monitoring for Myocardial Revascularization***

1. ECG: V_5 most sensitive for myocardial ischemia; inferior lead II for rhythm monitoring and inferior wall ischemia.
2. Arterial BP: Continuous invasive arterial BP monitoring and blood gas sampling by indwelling arterial catheter.
3. PAC: No evidence of improved outcome with PAC use. However, commonly used for treatment guidance in conjunction with TEE monitoring and for postoperative care in the ICU, particularly in patients with severely reduced ventricular function and those with pulmonary hypertension.
4. TEE: Recommended for all cardiac operations. TEE can assist in pre-CPB evaluation of cardiac function, associated valvular lesions, and evaluation of atheromatous plaques in the aorta.
5. Temperature monitoring: Bladder or esophageal (ie, core temperature) and nasopharyngeal or tympanic (ie, brain temperature) are recommended for all CPB cases to minimize temperature gradients and cerebral hyperthermia during rewarming. For OPCABs, bladder temperature only is sufficient.
6. Foley placement for all patients.

BP, Blood pressure; *CPB*, cardiopulmonary bypass; *ECG*, electrocardiogram; *ICU*, intensive care unit; *OPCAB*, off-pump coronary artery bypass; *PAC*, pulmonary artery catheter; *TEE*, transesophageal echocardiography.

Arterial Pressure Monitoring

The radial artery usually is cannulated for BP monitoring during CABG. Choosing the best site for radial artery cannulation depends on surgery-specific considerations and institutional and practitioner preferences. Procedures such as previous transradial artery catheterization (TRAC), radial artery harvesting, or axillary CPB cannulation may influence the site chosen for invasive arterial pressure monitoring. The newer TRAC sheaths can be problematic for monitoring during emergency CABG, and they have been associated with many complications. The radial artery on the side of a previous TRAC procedure probably should not be used for monitoring purposes.

Radial arterial pressures have proved to be inaccurate immediately after hypothermic CPB. Substantial reductions in radial arterial pressure compared with aortic pressure have been reported in several clinical investigations and often require 20 to 60 minutes after CPB to resolve. Decreased forearm vascular resistance is thought to be responsible for this common phenomenon. This problem can be overcome by temporarily transducing the arterial pressure directly from the aorta by a needle or a cardioplegia cannula.

Central Venous Cannulation

Placement of a central venous pressure (CVP) catheter routinely is performed in cardiac anesthesia for right atrial pressure measurement and for infusing vasoactive drugs. Some centers routinely place two catheters (ie, large introducer and smaller CVP catheter) in the central circulation to facilitate volume infusion and vasoactive or inotropic drug administration.

Pulmonary Artery Catheterization

The use of a pulmonary artery catheter (PAC) in medical and surgical settings has declined steadily, mostly due to the increasing amount of data from large, randomized studies showing that major clinical outcomes (particularly death) are not changed by PAC use and that the adverse effects of PAC monitoring should be considered. During surgery for myocardial revascularization and in the intensive care unit (ICU) setting, patient outcomes are independent of PAC use despite the substantial amount of physiologic information obtained.

Judge and colleagues surveyed the members of the Society of Cardiovascular Anesthesiologists to assess current PAC use. The use of a PAC for myocardial revascularization was practice-dependent, with anesthesiologists in private practices using PACs for hemodynamic monitoring the most, followed by those in academic and government practice settings. Off-pump coronary artery bypass (OPCAB) and minimally invasive CABG procedures were more likely to be monitored with a PAC.

Patient risk factors that may warrant PAC placement include significant impairment of ventricular function, known pulmonary hypertension, and right-sided HF. The 2011 ACCF/ACC guideline for CABG surgery suggested that PAC placement can be useful in patients in cardiogenic shock or hemodynamically unstable patients.

Transesophageal Echocardiography

The earliest signs of myocardial ischemia include diastolic dysfunction followed by systolic regional wall motion abnormalities (RWMAs), which occur within seconds of acute coronary occlusion. Worsening of RWMAs after CABG is associated with an increased risk of long-term adverse cardiac morbidity and has been suggested as a prognostic indicator of adverse cardiovascular outcome. New RWMAs detected in the intraoperative period frequently may result from nonischemic or ischemic causes such as changes in loading conditions, alteration in electrical conduction in the heart, post-CPB pacing, myocardial stunning due to ischemia before or during weaning from CPB, or poor myocardial preservation. TEE is highly sensitive but lacks specificity for myocardial ischemia monitoring. Additional limitations apply because not all wall segments can be monitored continuously in real time and compared with preoperative findings.

Despite these limitations, TEE use in patients undergoing CABG can provide invaluable information beyond ischemia detection. TEE can assist in the pre-CPB evaluation of cardiac function, assessment and quantification of associated valvular lesions that may impact the surgical plan (eg, concomitant functional mitral regurgitation [MR], aortic stenosis), or CPB management (eg, aortic regurgitation).

The aorta can be assessed for the presence and severity of atheromatous plaques, and TEE can help to locate appropriate cannulation and cross-clamp sites or avoid the manipulation of the aorta altogether (ie, no-touch techniques). Cannulation techniques, including retrograde cardioplegia cannula positioning, a persistent left superior vena cava cannula (ie, retrograde cardioplegia problem), venous cannula positioning allowing unobstructed venous drainage, and an aortic cannula position in the aortic arch, can be assisted by TEE guidance. TEE can detect complications such as iatrogenic aortic dissection and can evaluate de-airing after release of the aortic cross-clamp. TEE monitoring can guide hemodynamic management after CPB, including the assessment of ventricular function, volume status, and the choice of and response to inotropic support.

The American Society of Anesthesiologists (ASA) and the Society of Cardiovascular Anesthesiologists (SCA) developed practice guidelines in 1996 for the perioperative use of TEE. The guidelines were updated in 2010, and the routine use of TEE was recommended for all cardiac or thoracic aortic surgery, including all CABG or OPCAB procedures. The ASA Task Force thereby acknowledged that TEE information could impact perioperative anesthesia, surgical management, and patient outcomes. A comprehensive TEE examination is recommended by the American Society of Echocardiography (ASA)/SCA Task Force before and after CPB or after completion of revascularization in OPCAB surgery.

Neuromonitoring

Stroke and neurocognitive dysfunction are feared complications associated with CABG, whether or not CPB is used, and they occur at a high enough rate that further improvements are needed. Although monitoring alone cannot change outcomes, early recognition of potentially harmful events and interventions with an associated outcome benefit may be useful. There is no consensus about which neuromonitoring modality should be selected. However, specialty societies have increasingly recommended neuromonitoring in an effort to decrease the incidence of poor neurologic outcomes associated with cardiac surgery, including CABG and OPCAB. The 2011 ACCF/AHA guideline for CABG surgery recommended central nervous system monitoring for patients undergoing myocardial revascularization (class IIb recommendation). However, they also recognized that more evidence demonstrating clear benefits was needed and that the effectiveness of detecting cerebral hypoperfusion based on the available data is uncertain.

Induction and Maintenance of General Anesthesia

The main considerations in choosing an induction technique for patients undergoing CABG are LV function and coronary pathology. No single approach to anesthesia for CABG is suitable for all patients. Most hypnotics, opioids, and volatile agents have

BOX 14.3 *Considerations for Anesthesia Induction and Maintenance During Myocardial Revascularization*

1. Anesthetic induction with tight control of hemodynamic parameters (ie, avoid tachycardia, hypotension), particularly in patients with left main or proximal LAD disease.
2. Fast-track anesthetic protocols aiming for early extubation are favored for most patients.
3. Given the increasing evidence for preconditioning effects, a potent volatile agent should be part of the anesthetic regimen. Avoid nitrous oxide because of the possibility of expanding gaseous emboli.
4. Maintain CPP without increasing myocardial oxygen demand (eg, phenylephrine, nitroglycerin; avoid tachycardia).
5. Antifibrinolytic therapy (ie, ε-aminocaproic acid or tranexamic acid) except in OPCAB patients. Aprotinin is no longer available in the United States.
6. Consider low tidal volume mechanical ventilation and no PEEP during LIMA dissection.
7. Heparin usually is administered before clamping the LIMA pedicle to avoid thrombosis. Papaverine, if injected retrograde into the LIMA by the surgeon, is frequently associated with hypotension.
8. Heparin administration (300–400 IU/kg) or as calculated by heparin titration (Hepcon) in CABG patients with CPB. ACT >480 seconds and/or heparin level >2.5 U/mL is required for institution of CPB.

ACT, Activated coagulation time; *CABG*, coronary artery bypass grafting; *CPB*, cardiopulmonary bypass; *CPP*, coronary perfusion pressure; *LAD*, left anterior descending coronary artery; *LIMA*, left internal mammary artery; *OPCAB*, off-pump coronary artery bypass; *PEEP*, positive end-expiratory pressure.

been used in different combinations for the induction and maintenance of anesthesia, with good results in the hands of experienced clinicians. Limiting the amount of opioids or use of short-acting drugs is encouraged for patients eligible for fast-tracking and early extubation. With modern cardioplegia techniques and assuming an uneventful intraoperative course, cardiac function typically is well preserved, and the goal should be to extubate the patient within 6 hours postoperatively (Box 14.3).

Anesthetic Agents

The cardiac effects of commonly used induction agents have been investigated over many years. Unraveling the direct or indirect effects of a particular drug on the heart and circulation is complex because overall effects are based on contractility, vascular tone, and response of the autonomic nervous system and baroreceptors.

Etomidate is often the preferred induction agent in patients with depressed cardiac function because it has minimal or no direct negative inotropic or sympathomimetic effects. Despite the observed hemodynamic stability, unwanted side effects are common. Significant pain during injection, particularly in a small superficial vein, is unpleasant for the patient and causes tachycardia and hypertension, both of which increase myocardial oxygen demand. Unless combined with an adequate amount of opioids, blunting of the adrenergic response to intubation is poor and may result in hypertension and tachycardia. Even a single dose of etomidate can inhibit adrenal mitochondrial hydroxylase activity, resulting in reduced steroidogenesis; however, outcome differences in cardiac surgery patients have not been documented consistently.

Propofol is commonly used as an induction agent in patients undergoing CABG, for anesthesia maintenance, and for sedation postoperatively in the ICU. A load-independent measure of contractility, at four different plasma concentrations (0.6–2.6 mg/mL) found no direct effect on contractility, although it lowered preload and afterload. Although there seem to be well-documented advantages for using inhalation anesthetics in patients at risk for myocardial injury, benefits of propofol also have been reported. Propofol has strong free radical–scavenging properties that, in one CABG study, appeared to attenuate myocardial lipid peroxidation. In a multicenter, prospective study comparing an inhalation-based anesthetic with total intravenous anesthesia in patients undergoing combined valvular and CABG surgery, no observed beneficial effect of sevoflurane on the composite end point of mortality, prolonged ICU stay, and troponin levels was found. A large metaanalysis that included 133 studies and 14,516 cardiac and noncardiac surgery patients found no difference in mortality when propofol was used.

Benzodiazepines are commonly used in patients undergoing CABG for preoperative sedation and in combination with a narcotic to induce anesthesia. Midazolam is very well tolerated, with minimal hemodynamic effects even in patients with severe cardiac dysfunction.

In the late 1970s, Stanley first reported the use of high doses of fentanyl for CABG, with and without supplemental benzodiazepines. Clinicians worldwide perceived the lack of histamine release to be a very favorable property and rapidly adopted fentanyl into their clinical practice.

Reports on the use of the more potent sufentanil appeared at the same time as fentanyl, although most studies were not reported until the late 1980s. It was also widely adopted, although there was concern about its very potent bradycardic effects at high doses, particularly when administered with nonvagolytic muscle relaxants.

In the mid-1990s, remifentanil was introduced, and, fueled by intense interest in fast-tracking (promoted in the same time frame), it was intensively investigated.

The previously described opioids are pure opioid agonists, and none provides complete anesthesia as defined by predictable dose-response relationships for suppression of the stress response and release of endogenous catecholamines (particularly norepinephrine), even with high serum concentrations. Hypertension and tachycardia commonly have been reported in response to induction or intubation and surgical stimuli (particularly with sternotomy). In current practice, anesthesia using only a high-dose opioid is rarely practiced. To provide complete anesthesia, the usual practice is to supplement opioids with inhaled or other intravenous agents. This permits a reduction in the total dose of opioid and, particularly with volatile agents, more rapid return of respiratory drive, facilitating early extubation.

Neuromuscular blocking agents have been used to produce adequate intubating conditions and muscle relaxation during CABG. Traditionally, pancuronium was advocated for use with high-dose narcotic techniques because it offset opioid-induced bradycardia. Especially in fast-track cardiac surgery, shorter-acting neuromuscular blocking agents have completely replaced pancuronium, allowing earlier extubation and ICU discharge.

Inhalation Anesthetics and Myocardial Protection

Inhalation anesthetics are routinely used in patients undergoing CABG due to the shift from using a high-opioid anesthetic to fast-tracking and because of mounting evidence that potent inhalation anesthetics protect the myocardium against ischemia by eliciting protective cellular responses similar to those seen with ischemic preconditioning.

There is evidence that pharmacologic agents such as potent inhalation anesthetics and opioids mimic the effects seen with ischemic preconditioning, a concept called *pharmacologic or anesthetic preconditioning.*

Several metaanalyses looked at preconditioning and mortality rates or long-term outcomes for patients undergoing cardiac surgery. In a metaanalysis that included only studies with sevoflurane and desflurane, Landoni and coworkers showed a reduction in mortality rates and the incidence of MI after cardiac surgery. In two other metaanalyses that also included isoflurane, no such benefit was seen. De Hert and colleagues showed that the best results for myocardial protection were achieved when sevoflurane was administered throughout the intraoperative period rather than immediately before the planned myocardial ischemic event.

The 2011 ACCF/AHA guideline for CABG surgery provided level A evidence for using volatile-based anesthesia for patients undergoing myocardial revascularization to reduce the risk of perioperative myocardial ischemia and infarction.

Role of Central Neuraxial Blockade

A balanced general anesthetic is still the most commonly used technique for patients undergoing CABG. However, there are many publications on the use of neuraxial techniques, particularly from Europe and Asia, for patients undergoing cardiac surgery. It has been long appreciated that thoracic sympathectomy has favorable effects on the heart and coronary circulation.

In the United States, medicolegal concerns about the rare but real danger of a devastating neurologic injury, the substantial logistic issues regarding placement of the catheter the night before surgery (most patients undergoing nonemergent CABG in the United States are admitted on the morning of surgery), and the potential for cancellation of a procedure in the event of a bloody tap during epidural catheter placement have limited this technique. The ubiquitous use of potent antiplatelet drugs in patients with CAD and the insufficient data regarding when to safely discontinue those drugs before thoracic epidural anesthesia and before catheter removal postoperatively are major concerns. The advent of fast-tracking may be a driving force (ie, ability to extubate faster and have a more comfortable patient with thoracic epidural anesthesia), although most evidence suggests that a wide variety of techniques can be used effectively to facilitate early extubation. The cardioprotective effects of volatile agents may be as effective as the beneficial effects of thoracic sympathectomy.

Myocardial Ischemia in Patients Undergoing Revascularization Surgery

In addition to providing anesthesia, a major concern of the anesthesiologist is the prevention and treatment of myocardial ischemia. The 2011 ACCF/AHA guideline for CABG surgery recommended that determinants in coronary perfusion (ie, heart rate [HR], diastolic pressure or mean arterial pressure [MAP], and right ventricular [RV] or LV end-diastolic pressure [LVEDP]) should be monitored to reduce the risk of perioperative ischemia. Monitoring relevant hemodynamic parameters, detecting myocardial ischemia and prompt treatment are of paramount importance for patients undergoing myocardial revascularization.

The main hemodynamic goals are to ensure an adequate coronary perfusion pressure (CPP; ie, diastolic BP minus LVEDP) and HR control; HR is the single most important treatable determinant of myocardial oxygen consumption. Table 14.1 summarizes the treatment of acute perioperative myocardial ischemia.

Fig. 14.7 demonstrates how hypertension (ie, increase in wall stress), even in the absence of tachycardia, as a response to surgical stress (eg, skin incision) can be associated with pulmonary hypertension, elevated pulmonary capillary wedge pressure (PCWP), and prominent A and V waves on the PCWP waveform. Signs of myocardial

Table 14.1 Acute Treatments for Suspected Intraoperative Myocardial Ischemia[a]

Associated Hemodynamic Finding	Therapy	Dosage
Hypertension, tachycardia[b]	Deepen anesthesia	
	Intravenous (IV) β-blockade	Esmolol, 20–100 mg ± 50–200 μg/kg/min prn Metoprolol, 0.5–2.5 mg Labetalol, 2.5–10 mg
	IV nitroglycerin	Nitroglycerin, 10–500 μg/min[c]
Normotension, tachycardia[b]	Ensure adequate anesthesia, change anesthetic regimen	
	IV β-blockade	β-Blockade, as above
Hypertension, normal heart rate	Deepen anesthesia	
	IV nitroglycerin or nicardipine	Nicardipine, 1–5 mg ± 1–10 μg/kg/min Nitroglycerin, 10–500 μg/min[c]
Hypotension, tachycardia[b]	IV α-agonist	Phenylephrine, 25–100 μg Norepinephrine, 2–4 μg
	Alter anesthetic regimen (eg, lighten)	
	IV nitroglycerin when normotensive	Nitroglycerin, 10–500 μg/min[c]
Hypotension, bradycardia	Lighten anesthesia	
	IV ephedrine	Ephedrine, 5–10 mg
	IV epinephrine	Epinephrine, 4–8 μg
	IV atropine	Atropine, 0.3–0.6 mg
	IV nitroglycerin when normotensive	Nitroglycerin, 10–500 μg/min[c]
Hypotension, normal heart rate	IV α-agonist/ephedrine	α-Agonist, as above
	IV epinephrine	Epinephrine, 4–8 μg
	Alter anesthesia (eg, lighten)	
	IV nitroglycerin when normotensive	Nitroglycerin, 10–500 μg/min[c]
No abnormality	IV nitroglycerin	Nitroglycerin, 10–500 μg/min[c]
	IV nicardipine	Nicardipine, 1–5 mg ± 1–10 μg/kg/min

[a]Ensure adequacy of oxygenation, ventilation, and intravascular volume status and consider surgical factors, such as manipulation of heart of coronary grafts.
[b]Tachyarrhythmias (eg, paroxysmal atrial tachycardia, atrial fibrillation) should be treated directly with synchronized cardioversion or specific pharmacologic agents.
[c]Bolus doses (25–50 μg) and a high infusion rate may be required initially.

ischemia (ie, ischemic MR) often resolve with administration of a nitroglycerin (NTG) infusion.

Intraoperative Treatment of Myocardial Ischemia

INTRAVENOUS NITROGLYCERIN

Since the introduction in 1976 by Kaplan of the V_5 lead to diagnose myocardial ischemia and intravenous NTG to treat it, the drug has been one of the mainstays for treating perioperative myocardial ischemia. Intravenous NTG acts immediately to reduce LV preload and wall tension, primarily by decreasing venous tone at lower

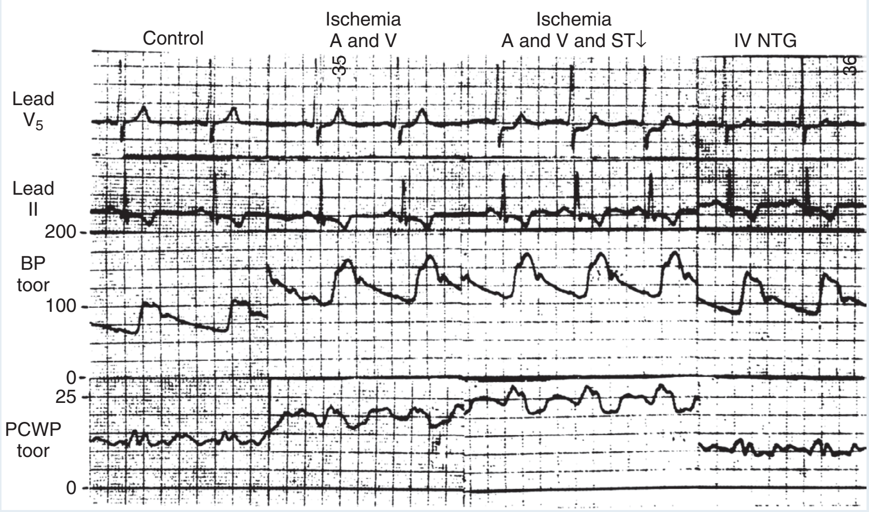
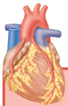


Fig. 14.7 Nitroglycerin *(NTG)* relieved postintubation intraoperative myocardial ischemia, as evidenced by large V waves in the pulmonary capillary wedge pressure *(PCWP)* tracing and then by ST-segment depression. *BP,* Blood pressure. (From Kaplan JA, Wells PH: Early diagnosis of myocardial ischemia using the pulmonary arterial catheter. *Anesth Analg*. 1981;60:789.)



BOX 14.4 ***Intraoperative Use of Intravenous Nitroglycerin***

Hypertension
Elevated pulmonary artery pressure
New-onset AC and V waves (ischemic mitral regurgitation)
Acute ischemia (ST changes >1 mm)
New regional wall motion abnormalities on transesophageal echocardiography
Diastolic dysfunction
Systolic dysfunction (with adequate coronary perfusion pressure)
Coronary artery spasm

doses, and at larger doses, it decreases arterial and epicardial coronary arterial resistance. It is most effective in treating acute myocardial ischemia with ventricular dysfunction accompanied by sudden elevations in LV end-diastolic volume, LVEDP, and pulmonary arterial pressure (PAP). The elevations in LV preload and wall tension further exacerbate perfusion deficits in the ischemic subendocardium and usually respond immediately to NTG.

In the pre-CPB period and during OPCAB, NTG is used to treat signs of ischemia such as ST-segment depression, hypertension uncontrolled by the anesthetic technique, ventricular dysfunction, and coronary artery spasm (Box 14.4). During CPB, NTG can be used to control the MAP, but only about 60% of patients are responders because of alterations of the pharmacokinetics and pharmacodynamics of the drug with CPB. Factors contributing to the reduction of its effectiveness include adsorption to the plastic in the CPB system, alterations in regional blood flow, hemodilution, and hypothermia. After revascularization, NTG is used to treat residual ischemia or

BOX 14.5 ***Uses of Intravenous Nitroglycerin on Termination of Cardiopulmonary Bypass***

- Myocardial ischemia or stunning
- Diastolic dysfunction
- Elevated pulmonary artery pressure, pulmonary capillary wedge pressure, central venous pressure, pulmonary vascular resistance, systemic vascular resistance
- Increased coronary perfusion pressure along with a vasopressor
- Prevention of arterial graft spasm (ie, radial artery graft)
- Coronary artery spasm
- Reinfusion of oxygenator volume

coronary artery spasm, reduce preload and afterload, and it may be combined with vasopressors (eg, phenylephrine) to increase the CPP when treating coronary air embolism (Box 14.5).

Intravenous NTG has been compared with other vasodilators such as nitroprusside and calcium channel blockers. Kaplan and Jones first demonstrated that NTG was preferable to nitroprusside during CABG. Both drugs controlled intraoperative hypertension and decreased myocardial oxygen consumption, but NTG improved ischemic changes on the ECG, whereas nitroprusside did not. Nitroprusside decreased CPP or produced an intracoronary steal in about one-third of patients with myocardial ischemia.

CALCIUM CHANNEL ANTAGONISTS

Nicardipine is a short-acting dihydropyridine calcium antagonist similar to nifedipine, but it possesses a tertiary amine structure in the ester side chain. It has highly specific modes of action, which include coronary antispasmodic and vasodilatory effects and systemic vasodilation. Among the calcium antagonists, nicardipine is unique in its consistent augmentation of CBF and its ability to induce potent vasodilator responses in the coronary bed. Nicardipine produces minimal myocardial depression and significantly improves diastolic function in patients with ischemic heart disease. Despite these beneficial properties, nicardipine is typically not the primary choice in treating myocardial ischemia during CABG.

Clevidipine was introduced for the treatment of perioperative hypertension. It is an ultrashort-acting, intravenously administered, dihydropyridine calcium channel blocker that acts as an arterial-selective vasodilator, and its action is rapidly terminated by blood and tissue esterases. In a randomized, double-blind, placebo-controlled, multicenter trial of the drug in patients undergoing cardiac surgery, clevidipine effectively reduced arterial BP. Like nicardipine, it could be used if NTG does not control the BP.

β-BLOCKERS

Hypertension, tachycardia, arrhythmias, and myocardial ischemia from sympathetic stimulation are common occurrences in the perioperative period. Despite the benefits of early use of β-blockers in the treatment of myocardial ischemia, the relatively long half-life and prolonged duration of action of previously available β-blockers had significantly limited their use during surgery and the immediate postoperative period. However, with the introduction of esmolol in the late 1980s, an ultrashort-acting cardioselective β_1-blocker with a half-life of 9 minutes became available. Esmolol was soon adopted by many clinicians for the prevention and treatment of myocardial ischemia. A mean esmolol dose of 17 ± 16 mg/min, with a range of 8 to 24 mg/min, was found to be effective in alleviating chest pain while increasing cardiac output in patients with unstable angina.

It was shown that esmolol was effective in treating acute myocardial ischemia, even in patients with poor LV function (ie, increased PCWP of 15–25 mm Hg). Esmolol was infused in doses up to 300 μg/kg per minute and produced decreases in HR, BP, and cardiac index. However, the PCWP was not significantly altered by the drug infusion. Even in the setting of moderate LV dysfunction, esmolol can safely reduce BP and HR in patients with acute myocardial ischemia.

Because of the favorable pharmacologic properties and encouraging clinical findings, esmolol was soon used frequently during CABG to treat hypertension and tachycardia and to prevent myocardial ischemia. It is usually given as a test dose of 20 mg IV. An infusion can then be used.

The Immediate Postoperative Period

Sedation

Patients usually are sedated to facilitate transport to the ICU and during the immediate postoperative period until extubation criteria are fulfilled. Dexmedetomidine, propofol, and midazolam are intravenously administered agents with favorable properties in this setting.

α_2-Adrenergic receptor agonists have unique properties (Box 14.6) that explain their increasing use in some cardiac surgery centers. In 1999, the FDA approved dexmedetomidine for continuous (up to 24 hours) intravenous sedation in the ICU. It is a more selective α_2-adrenoceptor agonist than clonidine, and exhibits central sympatholytic and peripheral vasoconstrictive effects. Intravenous bolus administration causes a transient increase in MAP and systemic vascular resistance due to stimulation of peripheral α- and β_2-adrenergic receptors in vascular smooth muscle. A continuous infusion (0.2–0.8 μg/kg per hour) has dose-dependent hemodynamic effects; most

BOX 14.6 ***α_2-Agonist Properties***

Sedation
Anxiolysis
Analgesia
Hemodynamic stability
Central sympatholytic effect
Decreased blood pressure and heart rate
Decreased perioperative oxygen consumption
Decreased plasma catecholamine levels
Decreased incidence of tachyarrhythmias
Prevention of histamine-induced bronchoconstriction
Treatment and prevention of postoperative shivering
Sedation in patients with postoperative delirium
Blunting of withdrawal symptoms in drug and alcohol addicts
Possible inhibition of inflammatory response

consistently decreases in HR, plasma catecholamine levels, and MAP. Dexmedetomidine may be a useful agent in the early postoperative period because its sedative properties are associated with minimal respiratory depression and appear to mimic natural sleep patterns. When administered continuously in postoperative patients, it caused no changes in respiratory rate, oxygen saturation, arterial pH, and arterial carbon dioxide (CO_2) tension compared with placebo. Patients usually were effectively sedated but still arousable and cooperative in response to verbal stimulation. Due to its analgesic properties, it significantly reduced additional opioid analgesia requirements in mechanically ventilated patients in the ICU.

Propofol has been used extensively intraoperatively and for sedation in the ICU. Several studies compared propofol and dexmedetomidine in the postoperative period after surgery. Dexmedetomidine reduced the requirement for opioid analgesia, but for patients after myocardial revascularization, it reduced HR more than propofol, whereas the arterial BP did not differ between the two groups.

A multicenter, randomized study compared a dexmedetomidine-based sedation regimen with propofol sedation after CABG in the ICU. Although there were no differences in time to extubation, the investigators found a significantly reduced need for additional analgesics (ie, propofol-sedated patients required four times the mean dose of morphine), antiemetics, and diuretics and they had fewer episodes of tachyarrhythmias requiring β-blockade (ie, ventricular tachycardia in 5% of the propofol-sedated group vs none in the dexmedetomidine group). However, hypotension was more common in the dexmedetomidine group compared with the propofol-sedated patients (24% vs 16%). Approximately 25% of the dexmedetomidine-associated hypotension occurred in the first hour of the study, particularly during or within 10 minutes after the loading infusion of 1 μg/kg. To avoid hypotension seen with a large loading dose of dexmedetomidine, loading doses are infrequently administered in clinical practice, but a continuous maintenance dose is started earlier to achieve appropriate plasma levels at the time of patient transfer from the operating room.

Coronary Artery and Arterial Conduit Spasm

There have been numerous descriptions of this complication. Spasm usually has been associated with profound ST-segment elevation on the ECG, hypotension, severe dysfunction of the ventricles, and myocardial irritability. Many hypotheses have been put forward to explain the origin of coronary artery spasm (Fig. 14.8). The underlying mechanism may be similar to the coronary spasm seen with Prinzmetal variant angina.

Therapy is usually effective with a wide range of vasodilators such as NTG, calcium channel blockers, milrinone, or combinations of NTG and calcium channel blockers. Arterial grafts with a vessel such as the left internal mammary artery (LIMA) and particularly radial artery grafts are prone to spasm after revascularization, and prevention and recognition are crucial to prevent serious complications.

Fast-Track Management for Coronary Artery Bypass Grafting

Although the fast-track clinical pathway encompasses a variety of perioperative and after-discharge management strategies, early extubation is the one that has received the greatest attention (Box 14.7). Early extubation is acknowledged as a key component of the fast-track clinical pathway and one that was considered the most radical change in practice during the peak of scrutiny of the fast-track pathway in the middle to late 1990s (Box 14.8).

The rigorous, randomized, controlled trial reported by Cheng and associates in 1996 ($N = 100$), in which mean time to extubation was 4.1 hours, is recognized as the most influential of the contemporary studies of early extubation. Reports of successful use of fast-tracking in a variety of patient populations have been reported

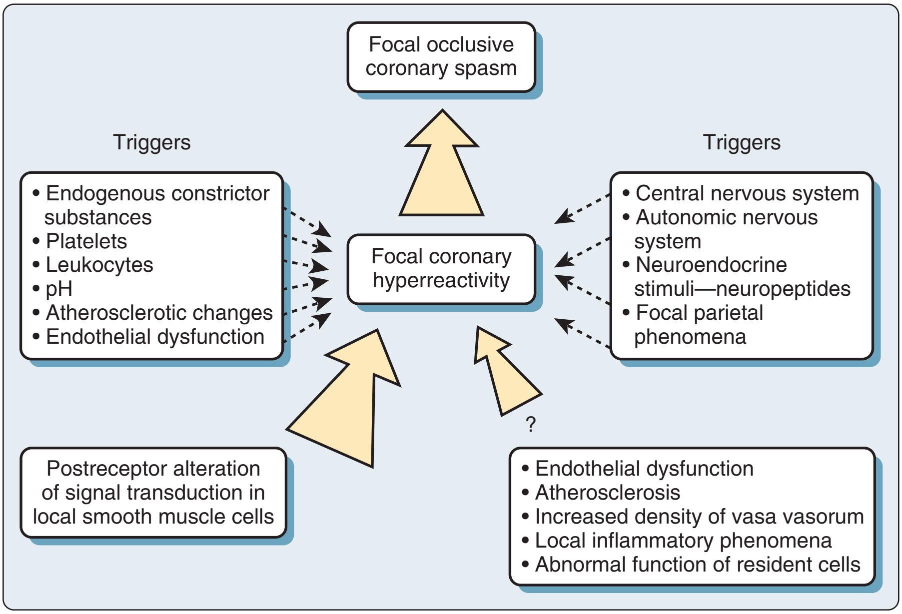
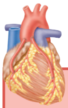


Fig. 14.8 Schematic representation of the pathogenesis of coronary artery spasm.



BOX 14.7 ***Perioperative Goals of Fast-Track Management***

Preoperative education
Same-day admission whenever possible
Anesthetic technique tailored to early extubation
Effective postoperative analgesia
Flexibility in the use of recovery areas (eg, postanesthesia care unit instead of intensive care unit)
Protocol-driven care
Early mobilization
Early intensive care unit and hospital discharge
Follow-up (eg, telephone, office visits) after hospital discharge
Interdisciplinary continuous quality improvement strategies

since, including academic, private, elderly, rural settings, and Veterans Affairs patients from the United States and many other countries.

The first metaanalyses of early extubation reported were based on accumulated data from randomized, controlled trials. It reviewed studies in which fast-tracking was defined as use of reduced opioid dosing (ie, fentanyl ≤20 µg/kg) with stated intention to attempt extubation in less than 10 hours postoperatively. They identified 10 trials (N = 1800) with most involving CABG patients from 1989 to 2002. The fast-track groups had shorter times to extubation (by 8.1 hours), with no significant differences in major morbidity or mortality rates and only one instance of reintubation. ICU LOS was reduced by 5.4 hours, although hospital LOS was not shortened.

BOX 14.8 ***Suggested Criteria for Early Extubation***

Body temperature >35°C
Normal acid-base status
Stable hemodynamics on minimal inotropic support
Adequate hemostasis with decreasing or stable mediastinal drainage
Stable cardiac rhythm
Spontaneous respiratory rate and adequate tidal volumes and inspiratory force
Chest radiograph without major abnormalities (eg, minimal atelectasis)
Adequate urine output
Adequate reversal of neuromuscular blockade
Awake, alert, cooperative, and moving all extremities

Some centers have adopted an even more aggressive form of fast-tracking. Walji and colleagues coined the term *ultrafast-tracking* to describe their practice and reported a 56% hospital discharge rate by postoperative day 4 and 23% discharge rate by postoperative day 2, although the readmission rate was 3.9%, but there was no early mortality. Ovrum and associates from Norway reported a cohort of 5658 patients with CABG, 99% of whom were extubated by 5 hours (median, 1.5 hours), with a 1.1% reintubation rate. More than 99% of patients were transferred to the ward the next morning.

CORONARY ARTERY BYPASS GRAFTING WITHOUT CARDIOPULMONARY BYPASS

The inherent risks of CPB and aortic cross-clamping continued to be a major factor in CABG morbidity and mortality. Avoiding CPB altogether seemed to offer a solution. It was not until the middle to late 1990s, when surgical researchers developed efficient mechanical stabilizer devices that minimized motion around the anastomotic site, that OPCAB surgery gained more widespread interest.

The pace and tempo of OPCAB surgery differs substantially from that of conventional CABG. Surgical manipulations involve a variety of geometric distortions of the cardiac anatomy, with resulting hemodynamic effects. Communication between all members of the surgical team and anticipation of these changes are vitally important to minimize resulting adverse hemodynamic effects on the heart and other organs. Significant hemodynamic changes that cannot be reversed may necessitate emergent conversion to CPB at any time during OPCAB surgery.

Cardiovascular Effects of Off-Pump Coronary Artery Bypass Grafting

Hemodynamic changes encountered during OPCAB involve the two independent variables of distortion of the right or left atria and ventricles by stabilizer and suspension devices and the effects of myocardial ischemia during anastomosis. The ability to expose the posterior surface of the heart to access the posterior descending and the circumflex vessels using suction devices placed on the apex or anterolateral wall of the heart, pericardial retraction sutures, slings, or other techniques without producing

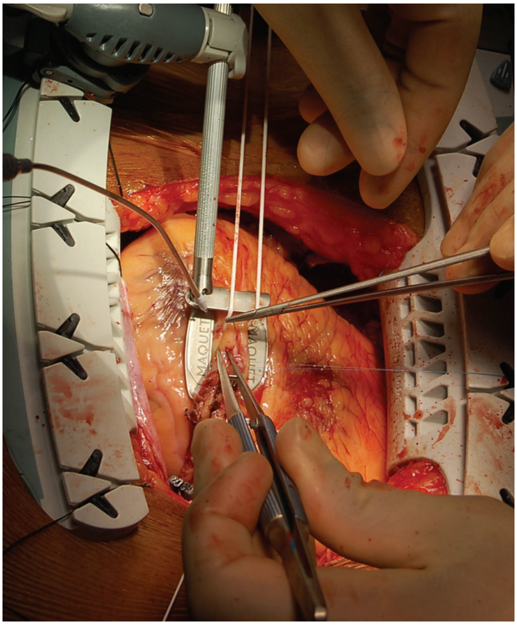


Fig. 14.9 Image depicting left anterior descending (LAD) artery anastomosis during off-pump coronary artery bypass grafting using a left internal mammary artery (LIMA) graft. The view is from the head of the patient. The Maquet mechanical stabilizer (Maquet, Wayne, NJ) is in place along with vascular snare sutures used to transiently occlude the artery. The LIMA is being anastomosed to the LAD, assisted by use of pressurized and heavily humidified carbon dioxide ("mister blower" metal cannula) to facilitate visualization of the vessel lumen. (Courtesy Alexander Mittnacht, MD, Mount Sinai School of Medicine, New York, NY.)

major hemodynamic compromise is critical for multivessel application of OPCAB surgery. Lifting of the heart to work on the posterior vessels commonly is referred to as *verticalization*, in contrast to *displacement* for the LAD and diagonal anastomoses (Figs. 14.9 through 14.11).

The effects of positional maneuvers, including verticalization of the heart, have been investigated. Most data have been obtained from patients with normal or only mildly depressed ventricular function without significant valvular disease with the Octopus stabilizer in the Trendelenburg position, right ventricular end-diastolic pressure increased in each position, with the greatest increase occurring with exposure of the circumflex vessels. This position was associated with the greatest deterioration of stroke volume (approximately 29% vs 22% for PDA and vs 18% for LAD). When comparing patients with EFs of more than or less than 40%, there were nonsignificant trends toward greater reductions in MAP and cardiac output with lower EF.

Mishra and colleagues have reported large-scale, prospective observational data on patients undergoing OPCAB surgery. TEE and PAC were used in all patients, and approximately 40% were considered high risk. Verticalization for exposure of the posterior wall was associated with a reduction in MAP of 18%, an increase in CVP of 66%, and a reduction in stroke volume of 36% and cardiac index of 45%. New RWMAs were common (60%), and global function decreased in a similar proportion. Their practice involved the use of inotropes during this period (79% vs 22% for the anterior wall). However, only 11% required intraaortic balloon pump (IABP), and 0.7% required CPB.

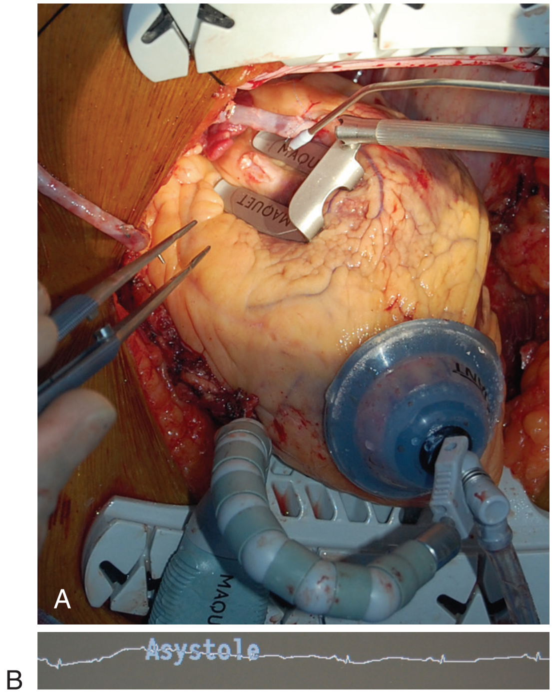


Fig. 14.10 (A) Posterior descending artery (PDA) anastomosis during off-pump coronary artery bypass grafting (CABG) uses a saphenous vein graft. The view is from the head of the patient. The Maquet access device (Maquet, Wayne, NJ) uses suction to position the heart (ie, verticalization) for easy access to the inferior surface of the left ventricle. The stabilizer is in place, and the anastomosis to the PDA is being performed. (B) Characteristic electrocardiographic (ECG) tracing during verticalization of the heart facilitates exposure of the PDA for anastomosis during off-pump CABG. Heart manipulations modify the positional relationship between the heart and surface electrodes. The shape of the tracing is altered, and the amplitude is reduced. The low-voltage electrocardiogram is interpreted by the device as asystole, an audible alarm sounds, and the practitioner is alerted with *Asystole* next to the ECG tracing. (Courtesy Alexander Mittnacht, MD, Mount Sinai School of Medicine, New York, NY.)

Specific Anesthetic Considerations in Patients Undergoing Off-Pump Coronary Artery Bypass Grafting

The anesthesia technique used for patients undergoing OPCAB surgery does not differ much from on-pump CABG (Box 14.9). The anesthesia technique should be tailored to the individual patient and, among other factors, it depends on the indication for OPCAB surgery. Fast-tracking, including early ICU and hospital discharge, is frequently a goal associated with OPCAB surgery, particularly for patients with adequate LV function. Patients with advanced age, significant ascending aortic disease, poor LV function, and multiple comorbidities may be scheduled for OPCAB surgery to avoid aortic cross-clamping, and a single LIMA-to-LAD anastomosis is sometimes performed.

A challenge during OPCAB surgery can be the hemodynamic changes encountered during positioning of the heart. PAP, PCWP, and CVP typically are increased during this phase; the occurrence of large V waves should alert the practitioner to acute ischemia or MR. Wall motion abnormalities and acute, significant MR frequently are seen on

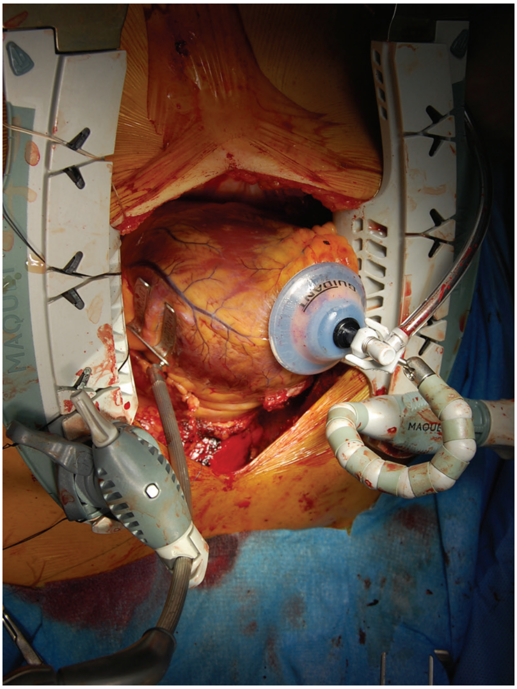


Fig. 14.11 First obtuse marginal anastomosis during off-pump coronary artery bypass grafting using a saphenous vein graft. The view is from the head of the patient. The previously completed left internal mammary artery to left anterior descending anastomosis is seen. The Maquet access device (Maquet, Wayne, NJ) uses suction to position the heart (ie, verticalization) for easy access to the circumflex coronary artery system. (Courtesy Alexander Mittnacht, MD, Mount Sinai School of Medicine, New York, NY.)

BOX 14.9 *Anesthetic Considerations for Off-Pump Coronary Artery Bypass Surgery*

1. Use standard monitoring, including invasive arterial blood pressure monitoring and central venous access.
2. A PAC should be considered in patients with poor LV function or significant mitral regurgitation.
3. TEE is recommended for all patients undergoing OPCAB surgery, unless contraindicated.
4. Use warming devices to maintain normothermia.
5. Dose of heparin according to institutional or surgeon's preference.
6. Fast-tracking, including early extubation, is often a goal in OPCAB surgery.
7. A neuraxial anesthesia technique may be used for postoperative analgesia or as the primary anesthetic technique. The patient must be carefully evaluated for absolute contraindications (eg, potent antiplatelet regimens).
8. Hemodynamic compromise may occur with positioning of the heart or stabilizer application. Positional maneuvers, volume administration, and vasoactive medications are used to maintain hemodynamic stability. CPB always should be immediately available.

CPB, Cardiopulmonary bypass; *LV*, left ventricular; *OPCAB*, off-pump coronary artery bypass grafting; *PAC*, pulmonary artery catheter; *TEE*, transesophageal echocardiography.

TEE. Exacerbation or new onset of MR may be related to structural changes from positioning the heart (eg, annular distortion), stabilizer application, or ischemia.

Hemodynamic compromise during OPCAB surgery can be managed with Trendelenburg positioning, volume administration, and temporary vasoconstrictor administration to maintain CPP during distal anastomosis. Opening of the right pleural space may accommodate the right ventricle, relieving the compression and improving hemodynamics. The right limb of the sternal retractor should be routinely elevated on a rolled towel to create space and avoid compressing of the right atrium or right ventricle against the right sternal border. Similarly, the right-sided pericardial traction sutures must be loosened when the heart is rotated to the right to avoid compression of the hemodynamically vulnerable right atrium and right ventricle against the right pericardial edge. Maintaining the CPP is critical during distal coronary anastomosis, and MAP is typically kept above 80 mm Hg during this phase.

Vasoconstrictor and volume therapy are preferred with inotrope use only in cases of severe hemodynamic compromise. In the setting of ongoing ischemia, the greater increase in oxygen demand with inotropes may place the patient at substantial risk for myocardial injury. In the setting of significant MR not responsive to antiischemic treatment, further increasing the afterload may worsen the clinical picture. Positive inotropic medications are then temporarily indicated if the surgeon cannot correct the position of the heart during critical phases of surgical anastomosis. The surgeon may or may not place temporary intracoronary shunts to allow distal coronary perfusion. There are controversial data and opinions about whether shunts have a clinical benefit in providing myocardial protection or instead cause endothelial damage.

CPB should always be immediately available during OPCAB surgery in case the hemodynamic situation cannot be managed pharmacologically. A lower arterial BP typically is preferred during the proximal (aortic) anastomosis to avoid complications seen with partial aortic clamping (ie, aortic side-clamp). Automated suture devices and techniques that eliminate aortic cross-clamping are being used. Avoidance of aortic partial clamping has been associated with a striking reduction in cerebral emboli and neurologic events during OPCAB. Regardless of the specific technique or device used, the MAP should be kept around 60 mm Hg during manipulation of the aorta and proximal anastomosis. Vasodilators such as NTG are frequently administered and titrated to achieve this goal.

Because CPB with a heat exchanger is not available for maintaining a target temperature, patients are at increased risk for hypothermia during OPCAB surgery. This is particularly problematic if fast-tracking with early extubation is the goal. The room temperature should be adjusted accordingly, and patient-warming devices should be applied.

Anticoagulation in patients undergoing OPCAB surgery is an area of controversy, and the topic always should be discussed with the surgeon before anesthesia induction. Some surgeons prefer low-dose heparinization (eg, 100–200 U/kg of heparin) with a target-activated coagulation time (ACT) of 250 to 300 seconds, whereas others may choose full heparinization (eg, 300 U/kg) during the procedure. The ACT is measured every 30 minutes, and heparin is administered accordingly to maintain the target ACT.

Outcomes for Off-Pump Coronary Artery Bypass Grafting

Although the literature base is increasing, the final word about differences in outcomes and which patients may benefit from OPCAB has not been written. This is not surprising given the technical challenges of OPCAB surgery and highly operator-dependent outcomes, which are difficult to account for even in large, prospective, randomized trials.

A metaanalysis of randomized trials by Cheng and associates found no significant differences in 30-day or 1- to 2-year mortality rates, MI, stroke (at 30 days and 1 to 2 years), renal dysfunction, need for IABP, wound infection, or reoperation for bleeding or reintervention (for ischemia). OPCAB was associated with significant reductions in AF (odds ratio [OR] = 0.58), numbers of patients transfused (OR = 0.43), respiratory infections (OR = 0.41), need for inotropes (OR = 0.48), duration of ventilation (weighted mean difference [WMD] of 3.4 hours), ICU LOS (WMD of 0.3 day), and hospital LOS (WMD of 1.0 days). Changes in neurocognitive dysfunction were not different in the immediate postoperative period; they were significantly improved at 2 to 6 months (OR = 0.57), but there were no differences seen at 12 months.

The critical issue of graft patency was addressed in only four studies, which varied substantially with regard to when assessment occurred (ie, 3 months in two and 12 months in two studies). Only one study reported a difference (ie, reduction in circumflex patency with OPCAB). Because of the small numbers of patients, the overall data for this category were considered inadequate for metaanalysis.

A working group of the AHA Council on Cardiovascular Surgery and Anesthesia analyzed the then-current literature and several small metaanalyses, although not the same ones as Cheng and coworkers. In an informal manner, they concluded that OPCAB probably was associated with less bleeding, less renal dysfunction, less short-term neurocognitive dysfunction (especially in patients with calcified aortas), and shorter hospital LOS. However, they also observed that it is more technically demanding, has a greater learning curve, and may be associated with lower rates of long-term graft patency. Perhaps related to the greater technical demands, surgeons appear to place fewer grafts compared with on-pump CABG, and incomplete revascularization may influence long-term outcomes. Puskas and colleagues reviewed 12,812 patients with CABG (1997–2006) and compared in-hospital major adverse events and long-term survival after OPCAB versus on-pump CABG. Long-term (10-year follow-up) outcomes did not differ significantly between on-pump and off-pump patients. OPCAB was associated with significant reductions in short-term outcomes such as operative mortality, stroke, and major adverse cardiac events. Further data analysis showed that short-term outcome (ie, operative mortality rate) did not differ between the two groups for patients at low risk (ie, The Society of Thoracic Surgeons [STS] predicted risk of death), whereas lower mortality rates were found for OPCAB surgery in high-risk patients.

MINIMALLY INVASIVE CORONARY ARTERY SURGERY

First reported in 1967, minimally invasive direct coronary artery bypass (MIDCAB) was performed with a limited left thoracotomy and LIMA-to-LAD graft on a beating heart. In the subsequent five decades, coronary artery surgery through a midline sternotomy has become the most commonly used approach. In the earlier years of cardiac surgery, this involved a large midline incision with associated complications such as wound infection and brachial plexus injury. Less invasive techniques were sought and developed with the goals of avoiding these complications, faster patient recovery, earlier hospital discharge, and improved patient satisfaction (eg, cosmetically more appealing incision). The following terminology is a sample of what is being used to describe the various surgical approaches.

The original term *MIDCAB* refers to LIMA takedown and anastomosis to the LAD through a small anterior thoracotomy. It can be performed off-pump or on-pump with femoral cannulation. Thoracoscopic and robotic techniques have been developed to avoid chest wall retraction and associated complications. Experience with robotically assisted CABG is limited, and clear outcome benefits have not been reported. Because of limited access to the coronary artery system using this approach, the procedure is often combined with percutaneous revascularization using coronary stents (ie, hybrid coronary revascularization). The hybrid approach is gaining popularity for selected patients with complex proximal-ostial LAD stenosis and typically one other lesion in a non-LAD vessel that can be easily stented.

Totally endoscopic coronary revascularization (TECAB) describes complete surgical revascularization through small chest wall incisions using thoracoscopic instruments and a robot to access coronary lesions that are not close to the chest wall incision. The procedure can be performed with or without CPB; the latter is called *beating-heart TECAB*. Endoscopically assisted CABG (EndoACAB) was developed to avoid the high costs associated with robotic use. In place of expensive robotic equipment, EndoACAB uses thoracoscopic and nondisposable instruments to harvest the LIMA. The coronary anastomosis is performed on a beating heart.

Most minimally invasive coronary artery surgical techniques are technically demanding and require close cooperation by the multidisciplinary surgical team to plan the exact approach, including the type and location of surgical incision; on-pump versus off-pump, patient access during surgery (especially in robotic surgery); and goals of fast-tracking, including early extubation and adequate pain relief. Although a fast-track anesthesia technique often is preferred, anesthesia induction and maintenance do not differ from the approach used in a midline sternotomy (Box 14.10).

An important difference is the requirement for lung deflation on the side of the surgical incision during a beating-heart minimal thoracotomy or thoracoscopy approach. Lung separation techniques, including a double-lumen tube and bronchial blockers with a standard endotracheal tube, have been described. Alternatively, jet ventilation has been reported to facilitate surgical access. Additional challenges compared with thoracic surgery with one-lung ventilation are thoracic insufflation of CO_2, which is required for intrathoracic surgical instrument manipulation and access to surgical anastomosis on the heart, and its hemodynamic consequences. Insufflation pressures

BOX 14.10 ***Anesthetic Considerations for Minimally Invasive Coronary Artery Surgery***

1. Apply fast-track anesthesia techniques, including adequate postoperative pain management.
2. Intraoperative monitoring should include central venous access, invasive arterial pressure monitoring, and transesophageal echocardiography. In complex multivessel coronary artery revascularization, the benefits of pulmonary artery catheter monitoring may outweigh the risks.
3. Defibrillator pads are mandatory and need to be placed with regard to the exact location of surgical incisions.
4. Lung separation may be required for off-pump procedures.
5. Intrathoracic carbon dioxide insufflation can cause hemodynamic changes.
6. In prolonged procedures, measurements of adequate body perfusion and oxygen balance should be performed frequently.
7. Emergency conversion to an on-pump procedure and/or emergency sternotomy may be required.

are typically kept below 10 to 15 mm Hg; nevertheless, significant increases in CVP and PAP typically occur. RWMAs have been described with thoracic insufflation, as has decreased cardiac output at higher insufflation pressures. Fluid administration and vasoconstrictor or inotropic support are frequently used to maintain hemodynamic stability. Urine output, plasma lactate, and SvO_2 should be monitored frequently, especially during long procedures.

If hemodynamic stability cannot be maintained or is acutely compromised (including uncontrolled surgical bleeding), the use of femoral-femoral cannulation and prompt initiation of CPB can be lifesaving. Any otherwise unexplained rise in end-tidal CO_2 should alert the practitioner to increased CO_2 absorption from the positive-pressure thoracic insufflation. Sudden decreases in end-tidal CO_2 have been described with positive-pressure CO_2 insufflation in different settings and, if encountered, they should alert the practitioner to possible massive CO_2 embolization.

Due to the hemodynamic changes associated with thoracic inflation and prolonged one-lung ventilation in long surgical cases, adequate monitoring of hemodynamic and oxygenation parameters is considered prudent. TEE is recommended and, although outcome data are lacking, a PAC catheter is frequently inserted, especially if more than a single-vessel LIMA anastomosis is planned.

Access to the heart is limited, and defibrillator pads have to be placed before the patient is positioned and draped. This is further complicated by interference with surgical instruments and left chest wall incisions, and the defibrillator pad position may have to be modified accordingly. Because of the frequently cited advantages of early patient mobilization and hospital discharge, fast-track anesthesia is often part of the perioperative management strategy. A midline sternotomy is less painful for most patients compared with a small thoracoscopic incision with chest wall retraction. Adequate pain management is therefore mandatory in achieving fast-tracking goals for these patients. Long-acting intercostal nerve or other types of nerve blocks, administered before skin incision and redosed at the end of the surgical procedure, can facilitate overall anesthesia and pain management.

SUGGESTED READINGS

Bomb R, Oliphant CS, Khouzam RN. Dual antiplatelet therapy after coronary artery bypass grafting in the setting of acute coronary syndrome. *Am J Cardiol*. 2015;116:148.

Brinkman W, Herbert MA, O'Brien S, et al. Preoperative β-blocker use in coronary artery bypass grafting surgery: national database analysis. *JAMA Intern Med*. 2014;174:1320.

Cavallaro P, Rhee AJ, Chiang Y, et al. In-hospital mortality and morbidity after robotic coronary artery surgery. *J Cardiothorac Vasc Anesth*. 2015;29:27.

Chassot PG, van der Linden P, Zaugg M, et al. Off-pump coronary artery bypass surgery: physiology and anaesthetic management. *Br J Anaesth*. 2004;92:400.

Cheng DC, Bainbridge D, Martin JE, et al. Does off-pump coronary artery bypass reduce mortality, morbidity, and resource utilization when compared with conventional coronary artery bypass? A meta-analysis of randomized trials. *Anesthesiology*. 2005;102:188.

Collison SP, Agarwal A, Trehan N. Controversies in the use of intraluminal shunts during off-pump coronary artery bypass grafting surgery. *Ann Thorac Surg*. 2006;82:1559.

Coronary Revascularization Writing Group, Patel MR, Dehmer GJ, Hirshfeld JW, et al. ACCF/SCAI/STS/AATS/AHA/ASNC/HFSA/SCCT 2012 appropriate use criteria for coronary revascularization focused update: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, American Society of Nuclear Cardiology, and the Society of Cardiovascular Computed Tomography. *J Thorac Cardiovasc Surg*. 2012;143:780.

Curtis JA, Hollinger MK, Jain HB. Propofol-based versus dexmedetomidine-based sedation in cardiac surgery patients. *J Cardiothorac Vasc Anesth*. 2013;27:1289.

Daniel WT 3rd, Kilgo P, Puskas JD, et al. Trends in aortic clamp use during coronary artery bypass surgery: effect of aortic clamping strategies on neurologic outcomes. *J Thorac Cardiovasc Surg*. 2014;147:652.

De Hert S, Vlasselaers D, Barbe R, et al. A comparison of volatile and non volatile agents for cardioprotection during on-pump coronary surgery. *Anaesthesia*. 2009;64:953.
De Hert SG, Cromheecke S, ten Broecke PW, et al. Effects of propofol, desflurane, and sevoflurane on recovery of myocardial function after coronary surgery in elderly high-risk patients. *Anesthesiology*. 2003;99:314.
de Waal BA, Buise MP, van Zundert AA. Perioperative statin therapy in patients at high risk for cardiovascular morbidity undergoing surgery: a review. *Br J Anaesth*. 2015;114:44.
Judge O, Ji F, Fleming N, et al. Current use of the pulmonary artery catheter in cardiac surgery: a survey study. *J Cardiothorac Vasc Anesth*. 2015;29:69.
Landoni G, Biondi-Zoccai GG, Zangrillo A, et al. Desflurane and sevoflurane in cardiac surgery: a meta-analysis of randomized clinical trials. *J Cardiothorac Vasc Anesth*. 2007;21:502.
Landoni G, Greco T, Biondi-Zoccai G, et al. Anaesthetic drugs and survival: a Bayesian network meta-analysis of randomized trials in cardiac surgery. *Br J Anaesth*. 2013;111:886.
Landoni G, Guarracino F, Cariello C, et al. Volatile compared with total intravenous anaesthesia in patients undergoing high-risk cardiac surgery: a randomized multicentre study. *Br J Anaesth*. 2014;113:955.
Mishra M, Shrivastava S, Dhar A, et al. A prospective evaluation of hemodynamic instability during off-pump coronary artery bypass surgery. *J Cardiothorac Vasc Anesth*. 2003;17:452.
Myles PS, Daly DJ, Djaiani G, et al. A systematic review of the safety and effectiveness of fast-track cardiac anesthesia. *Anesthesiology*. 2003;99:982.
Pasin L, Landoni G, Nardelli P, et al. Dexmedetomidine reduces the risk of delirium, agitation and confusion in critically ill patients: a meta-analysis of randomized controlled trials. *J Cardiothorac Vasc Anesth*. 2014;28:1459.
Puskas JD, Kilgo PD, Lattouf OM, et al. Off-pump coronary bypass provides reduced mortality and morbidity and equivalent 10-year survival. *Ann Thorac Surg*. 2008;86:1139.
Shahian DM, O'Brien SM, Sheng S, et al. Predictors of long-term survival after coronary artery bypass grafting surgery: results from the Society of Thoracic Surgeons Adult Cardiac Surgery Database (the ASCERT study). *Circulation*. 2012;125:1491.
Stenger M, Fabrin A, Schmidt H, et al. High thoracic epidural analgesia as an adjunct to general anesthesia is associated with better outcome in low-to-moderate risk cardiac surgery patients. *J Cardiothorac Vasc Anesth*. 2013;27:1301.
Wagner CE, Bick JS, Johnson D, et al. Etomidate use and postoperative outcomes among cardiac surgery patients. *Anesthesiology*. 2014;120:579.
Wiesbauer F, Schlager O, Domanovits H, et al. Perioperative beta-blockers for preventing surgery related mortality and morbidity: asystemic review and meta-analysis. *Anesth Analg*. 2007;104:27.
Zhang X, Zhao X, Wang Y. Dexmedetomidine: a review of applications for cardiac surgery during perioperative period. *J Anesth*. 2015;29:102.